DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

FOOD & DRUG ADMINISTRATION
466 FERNANDEZ JUNCOS AVENUE
SAN JUAN, P.R. 00901-3223

HFC-31 10/16/97

4160

September 25, 1997

WARNING LETTER
SJN-97-25

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Terry Stecz
President
Whitehall Robins Healthcare
American Home Products Corporation
P.O. Box 310
Five Giralda Farms
Madison, NJ 07940-0874

Dear Mr. Stecz:

During an inspection of your drug manufacturing facility, Whitehall Laboratories P.R., Road #3 Km. 141.3, Guayama, PR conducted from June 9 to August 11, 1997, our investigators documented deviations from the Good Manufacturing Practice Regulations (Title 21, Code of Federal Regulations, Part 211) in conjunction with your firm's manufacture of tablets and capsules causing these drug products to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act, as follows:

1. Failure to reject a lot of drug product which did not meet established specifications in accordance with 21 CFR 211.165 (f) in that:

> A lot of Orudis* KT (ketoprofen) Caplets, Lot # 6XG288 was first analyzed for content uniformity on March 27, 1996, using HPLC #5. This test run was invalidated because of a technical error which occurred during the testing. The lot was next tested on April 2, 1996, again using HPLC #5 and out-of-specification result for one of ten tablets was obtained. The results of this test were invalidated because an operator on a subsequent shift observed a technical problem with HPLC #5 while using the machine. On April 3, 1996 an additional 20 tablets of lot # 6XG288 were tested for content uniformity, again using HPLC #5. During this testing run, three of the twenty tablets had out-of-specifications results. These results were invalidated

along with some, but not all, other tests run on HPLC #5 between March 27, 1996 and April 3, 1996 because there was a technical problem reported with this instrument. An additional content uniformity test was run for lot # 6XG288 on another HPLC and passing results were obtained at level 2. The lot was released based on these passing test results. After our inspection, your firm initiated 5 additional tests for content uniformity on this lot and obtained out-of-specification results for 2 tablets. On September 9, 1997, you initiated recall of the product from the market.

2. Failure to have adequate acceptance criteria for the testing conducted by the quality control unit in accordance with 21 CFR 211.165 (d) in that:

> In the incident described in #1 above, there was no record of justification for the decision to reject some data, including content uniformity test results for lot #XG288 and 4 other lots of Orudis KT caplet cores, while accepting other data, including at least 40 assay results for Orudis KT coated tablets and 20 content uniformity test results for other lots of Orudis KT caplet cores.

We acknowledge receipt of your letter, dated September 9, 1997. Your responses to FD-483 observations 2 and 8 were not adequate for the reasons mentioned under items 1 and 2 above. The responses to the FD-483 observations # 3, 4, 6 and 9 appear, if fully implemented, to adequately address the concerns of the investigators. With regard to FD-483 observation #1, we would suggest, if you decide to resume production of Orudis KT products, that you submit the blend uniformity and content uniformity validation data to the NDA reviewer at the Center for Drug Evaluation and Research for evaluation. With regard to FD-483 items #5 & 7, we request clarification of the statement: "Controls were added to the Laboratory Data Management System to add more security by not allowing a report to be printed at the supervisory level for approval when there are invalid or out-of-specification results." Our specific question with regard to this statement is how this change will affect the traceability and accountability of out-of-specification results.

The above identification of violations is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure adherence with each requirement of the Good Manufacturing Practice Regulations. Federal agencies are advised of the issuance of all warning letters about drugs so that they may take this information into account when considering the award of contracts.

Please notify the San Juan District office in writing within 15 working days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to prevent the recurrence of these or similar violations.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. These include seizure and/or injunction.

Your reply should be sent to the Food and Drug Administration, San Juan District Office, 466 Fernandez Juncos Ave., San Juan, Puerto Rico 00902-3223, Attention: Mary L. Mason, Compliance Officer.

Sincerely,

for Samuel Jones
District Director